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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/495,947	02/02/2000	Timothy P. Coleman	05270001AA	5493

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/495,947	Applicant(s) COLEMAN ET AL.
	Examiner Janice Li	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *4-9,14-23,26,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-13,24,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, drawn to a protein composition derived from DHBV, in Paper No.19 is acknowledged. The following issues are raised in the response to the restriction requirement, and will be addressed as following.

It is acknowledged that applicants correctly point out that claims 21 and 23 are drawn to a method, not a composition, which were inadvertently and improperly placed in group I; and claim 24 is drawn to a composition, not a method, which was inadvertently and improperly placed in group VI. Thus, only claims 1-3, 10-13, 24, 25, and 27 belong to the elected group I.

Applicants request clarification of separate utility for the subcombinations of groups I-IV, which have been indicated in Office action Paper #18 briefly, and will be further explained here. Each of the subcombinations is drawn to a combination of structurally different molecules, even though they all contain a duck HBV nucleocapsid particle, upon addition of the other component in the subcombination, the resulting composition becomes a structurally different molecule, which belongs to a distinct chemical entity. For example, a protein molecule is patentably distinct from a protein-polynucleotide hybrid molecule in chemical structures, mode of operations, and utilities. The composition of group II comprising a nucleic acid selected from a group consisting of SEQ ID Nos: 3-9 is used in the method of group V for delivering a nucleic acid to a subject in need thereof, but it is not used in the methods of group VI, drawn to delivery

of a protein. The composition of group I could be used as antigens in an immune assay, but the composition of group II comprising SEQ ID Nos: 3-9, coding region for several cytokines, would not be used in such an assay method.

Applicants further requested to traverse the restriction of groups I-IV on the ground(s) that simultaneous examination of the inventions of proposed groups I-VII would not present a serious burden to the Examiner, that the previous Examiner examined all of the inventions in one Office action. This is not found persuasive because it is maintained that each of the Inventions requires a separate search status and consideration. The inventions are mutually exclusive and independent products that could be used in many *in vivo* and *in vitro* processes. The additional components in compositions of Invention groups II-IV require distinct search criteria and technical considerations than the Invention of group I. In this Office action, searching and examining of group I alone, additional six new prior art references have been cited, these references should have been available at the time of issuing of the previous Office action (Paper #16). Thus, further search and examination of additional three to six groups would impose a serious burden on the Office. Further search for these groups would have certain overlap, but they are not co-extensive as indicated by the separate classifications. Therefore, it is maintained that these inventions are distinct due to their divergent subject matter and the restriction requirement is still deemed proper.

Concerning restrictions among groups V-VII, applicants cite M.P.E.P. 806.04 and 808.01, and argue that restriction is proper only to inventions claimed that are not connected in design, operation, or effect, and the Examiner has presented no argument

that the methods represented by proposed groups V-VII are significantly disparate. This is found not persuasive because the Examiner's argument was presented in Paper # 18, 2nd paragraph of page 4, which uses and cites M.P.E.P. 806.04 and 808.01 as the bases to determine whether the claimed inventions are independent and distinct. The paragraph starts with the criteria suggested in M.P.E.P. 808.01, and continues pointing out that groups V and VI are drawn to an *in vivo* method for stimulating an immune response, group VII is drawn to an *in vitro* method for preparation of a composition. Each of the groups differs either in the material (proteins or hybrids of nucleic acid and proteins) used in the process, the function of the process or the method steps (in vivo vs. in vitro). The different methods use material different substances and reagents; have different method steps, different modes of operation, distinct technical considerations and search criteria. Applicants have not specifically respond to the arguments with the factually evidence to indicate otherwise as MPEP required. Therefore, the restriction is still deemed proper.

Concerning the Examiner's assertion that Group VII and I or II are related as process of making and product made, but the products of groups I or II could be made with a different process, applicants require the Examiner to identifying any alternate process by which a claimed product may be manufactured. It is noted that restriction under MPEP § 806.05(f) does not require a two-way distinction. However, per applicants request, the specific alternative methods of making the products of groups I and II are numerous methods of chemical and genetic synthesizing and modification known in the art, which could be found in each of the cited prior art references in

sections under 35 U.S.C. 102, such as *Yang et al* (J Virol 1994;68:338-45) by insertion and deletion, *JP 07252300* by genetically recombination, *Weizacker et al* (Hepatol 1996;24-294-99) by terminal extension and truncation, and *Birkett et al* (US 6,231,864) by strategic chemical modification. Therefore, the requirement for restriction is still deemed proper and is therefore made **FINAL**.

Please **note** that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-29 are pending, however, claims 4-9, 14-23, 26, 28, and 29 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim.

Claims 1-3, 10-13, 24, 25, and 27 are under current examination.

Please note that previous rejections that rendered moot in view of the restriction or the amendment to claims will not be reiterated; and the arguments presented in Paper #17 would be addressed to the extent that they apply to the current or new grounds of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 10-13, 24, 25, and 27 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Mason et al* (J Virol 1980;36:829-36) and as evidenced by *Birkett* (US 6,231,864).

These claims are drawn to a composition comprising a plurality of recombinant nucleocapsid protein monomers, wherein the primary sequences of which are derived from duck hepatitis B virus, wherein said monomers are assembled to form a particle, wherein the nucleocapsid protein monomers includes at least a first and optionally a second hapten, wherein the two haptens are different from each other, and are causative agents of infectious diseases associated with viruses, parasites, fungi, bacteria, and cancer, wherein the two haptens are present on the same monomer (intrinsic mosaic), or on different monomers (extrinsic mosaic), wherein the composition

particularly drawn to a duck HBcAg and a hapten linked to said duck HBcAg, wherein the hapten is proteinaceous.

The amended claim 1 and 24 recite "recombinant" before nucleocapsid or duck. The specification defines the term "encompasses particles composed of recombinant monomers whose sequences are identical to those of native duck HBcAg, and also of recombinant monomers with variations in both the amino acid and/or the nucleic acid sequences of DHBcAg" (paragraph bridging pages 13 and 14). Thus, the claims encompass the cited art, because *Mason et al* disclose native duck HBcAg particles comprising at least two different haptens present on the same or different nucleocapsid protein monomers. Applicants argue in Paper #17 that "Mason does not disclose the assembly of recombinant nucleocapsid monomers as defined in the composition of amended claim 1". In response, it is the intrinsic property of hepatitis B core protein monomers to self-assemble into stable aggregates during HBV replication or when synthesized in the absence of other HBV gene products as taught by *Birkett* (column 3) and also *Schodel* (left column, page 92). Thus, in the absence of evidence to the contrary, *Mason et al* still anticipate the instant claims.

Claims 1, 2, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by *Yang et al* (J Virol 1994;68:338-45).

Yang et al teach mutants (recombinant) of DHBcAg by deletion and insertion mutations. They teach 3 out of 12 DHBV core protein mutations self-assembled to form core particles (2nd paragraph, page 342). The particle comprises at least one hapten of

DHBV core antigen associated with duck hepatitis infection, thus, *Yang et al* anticipate the instant claims.

Claims 1-3, 10-13, 24, 25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by *JP 07252300*. (10/3/95)

JP 07252300 teaches fusion proteins (recombinant) between duck HBcAg and human HBV comprising at least two different immunogenic haptens, the duck core antigen and various human HBV antigens, such as HBeAg and HBcAg (fig. 1, page 14), which are associated with hepatitis infection in the human and duck, thus, *JP 07252300* anticipates the instant claims.

Claims 1-3, 10-13, 24, 25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by *Weizacker et al* (Hepatol 1996;24-294-99).

Weizacker et al teach mutants (recombinant) of DHBcAg comprising small surface protein (2^{nd} hapten), various fragments of the viral polymerase at the amino- or carboxyl-terminals of the DHBV core protein (at least a 1^{st} hapten, intrinsic or extrinsic mosaic). The core and surface antigens are associated with hepatitis infection; thus, *Weizacker et al* anticipate the instant claims.

Claims 1-3, 10-13, 24, 25, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by *Birkett et al* (US 6,231,864).

Birkett teaches a composition comprising a modified HBV core protein or its aggregated nucleocapsid protein particles, pendently linked to a hapten (abstract), wherein the HBV include duck HBV (column 7, lines 56-57), wherein the hapten is any compound of interest for generating an immune response, such as a pathogen-related polypeptide hapten (proteinaceous, column 4, lines 34-41). *Birkett* teaches that HBV core protein monomers self-assemble into stable aggregates known as HBV core protein particles, that even after insertion mutations, the HBV core protein still are able to form core particles when foreign epitopes are cloned into the immunodominant loop region of HBc, thus could be used as a carrier for linking pathogenic hapten (column 3). They go on to teach, in addition to intrinsic mosaic, the composition comprising assembled HBV core protein where a plurality of the subunits are strategically modified hepatitis B core protein subunits (monomers) or a particle comprised of a mixture of strategically modified hepatitis B core protein subunits (extrinsic mosaic, column 5, lines 16-22). Therefore, *Birkett* anticipates the instant claims.

Claims 1, 2, and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by *Kock et al* (J Virol 1998;72:9116-20).

Kock et al teach mutants (recombinant) of DHBV nucleocapsids made by N-terminal extension or C-terminal truncation, and mutants formed nucleocapsid particles, thus, *Kock et al* anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 10, 11, 13, 24, 25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Schodel et al* (J Biotechnol 1996;44:91-6), in view of *Birkett* (US 6,231,864).

Schodel et al teach using HBcAg particle as vaccine carrier moiety for heterologous epitopes, such as circumsporozoite antigen, and *Salmonella typhimurium*, for enhancing immune response in a host (abstract). *Schodel et al* do not particularly teach the duck HBV. *Birkett* teach modifying core protein of the hepadnaviridae family for its broadly applicable immunogenicity, which family includes HBV of different species including human, woodchuck, and duck, etc (column 3, lines 6-11, and column 7, lines 56-57).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions taught by *Schodel et al and Birkett*, selecting a core protein from the species of interest of the hepadnaviridae family as taught by *Birkett,* with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
June 17, 2002

JAMES KETTER
PRIMARY EXAMINER